REMARKS

Reconsideration of the above application is respectfully requested.

Claims 1-18 have been rejected. Upon entry of the amendments herein, Claims 1, 3, 4, and 6-18 will be pending.

By this Amendment, claims 2 and 5 have been cancelled, and claims 1, 3, 6, 8, and 13 have been amended. In summary, the term "aryl-heterocyclic compound" has been restricted in the claims to zipasidone, including ziprasidone free base or any pharmaceutically acceptable ziprasidone salt or polymorph, and in claim 8 the term "viscosity agent" has been specified as a cellulose derivative. Accordingly, the amendments herein do not raise an issue of new matter.

Rejections under 35 U.S.C. 112

The Examiner has rejected claims 1-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner rejects claim 1 and all claims dependent thereon for inclusion of the term "aryl-heterocyclic compound", on the grounds that such term is not defined. Applicant respectfully traverses the Examiner's rejection on the grounds that this term is well understood to those of ordinary skill in the art. Specifically, Applicant refers the Examiner to pages 2 and 3 of the present specification wherein this term is specifically defined. However, in an interest to expedite prosecution of the present invention, Applicant has amended claim 1 to refer to the compound ziprasidone. Applicant therefore respectfully submits that the Examiner's rejection on this ground has been rendered moot, and he respectfully requests that the Examiner remove the objection on this ground.

The Examiner has rejected claims 1-18 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for formulation comprising viscosity agents, does not enable any person skilled in the art to make the invention commensurate in scope with these claims. The Examiner then proceeds to analyze the disclosure of the viscosity agents pursuant to *In re Wands*. More specifically, the Examiner argues that the state of the pharmacological art is high but that there is no absolute predictability in this area in that "The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting such broad term viscosity agents claimed in the invention." Additionally, the Examiner challenges the amount of direction or guidance present in the specification, alleging that the disclosure on page 5, lines 34-37, and page 6, lines 1-10, is insufficient to enable the use of these viscosity agents. Finally, the Examiner argues that the breadth of the claims is so large that each embodiment of the invention is required to be individually assessed to determine which viscosity agents exhibit the depot formulation desired pharmacological activity.

Applicant respectfully traverses the Examiner's rejection on the grounds that the claims as amended are fully enabled such that one of ordinary skill in the art would know how to practice the

invention. The invention relates to viscosity agents for obtaining a ziprasidone injectable depot formulation. It does not lie in selection of certain viscosity agents for achieving a ziprasidone injectable depot. Accordingly, Applicant should not be required to narrow the claimed invention when the viscosity agents are well established substances to a person of ordinary skill in the art. As to the discussion of the specific viscosity agents, Applicant challenges the Examiner's rejection of these terms. For one thing, significant experimentation that is routine is acknowledged as not offending the enablement standards (see, for example, In re Colianni, 561 F.2d 220, 224, 195 USPC 150, 153 (CCPA 1977)).

Rejections under 35 U.S.C. 102

The Examiner has also rejected claim 1, 2, 6 and 8 under 35 U.S.C. 102(b) as being anticipated by Tsai et al. U.S. Patent 6,228,875 on the grounds that the reference discloses administering an effective amount of ziprasidone and lists select viscosity agents in the application. Applicant respectfully traverses the Examiner's rejection on the grounds that the Examiner has misapplied the rules of anticipation. Specifically, it is not sufficient that the Examiner can find the various components of the invention in a reference. Anticipation requires that the single source must disclose all of the claim elements "arranged as in the claim" (Richardson v. Suzuki Motor Company, 9 U.S.P.Q. 2nd 913). Nowhere does Tsai et al. specifically refer to a formulation such as that contemplated by the present inventor. Specifically, two elements must co-exist in order to anticipate the claimed invention: namely, a *solubilized* ziprasidone (emphasis added) and a viscosity agent. Tsai et al. does not disclose these two elements coexisting together, and Tsai et al. does therefore not anticipate the claimed invention.

Furthermore, ziprasidone is listed as one in a multitude of agents that are useful for treating neuropsychiatric disorders. Also, in the specific compositions discussed in the Tsai reference, it is made known that the composition is to contain a list of specific amino acids. Finally, the compositions described are discussed in the form of optional excipients that may include a multitude of elements, only a few which are viscosity agents, but for the purposes of Tsai, are referred to as "disintegrators" or binders for tablets. In neither description are these excipients identified as useful for parenteral administration. Thus, Applicant respectfully submits that the application of Tsai for anticipation is inappropriate and respectfully requests that the Examiner remove the rejection on these grounds.

The Examiner has also rejected claims 1-5, 9, 10, 12 and 15 as anticipated under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (WO 97/418996). The Examiner stated that Johnson et al. discloses a formulation comprising an aryl-heterocyclic such as ziprasidone and a cyclodextrin inclusion of complex, an aqueous solution and organic solent and pharmaceutically acceptable salt of an aryl-heterocyclic compound. The Examiner stated that the amount of

recommended range for ziprasidone is 5-300 mgA/ml and a cyclodextrin in a wide range of concentration from 5% to 100% w/v.

Applicant respectfully traverses this rejection. As with the rejection made over Tsai et al., the Examiner appears to have looked for various components of the claimed invention, but has not found within Johnson et al. any disclosure of all of the elements arranged together as in the present claims. Since Johnson et al. does not disclose the particular arrangement of elements, i.e. a solublized ziprasidone in combination with a viscosity agent, Johnson et al. fails to anticipate the claimed invention. Accordingly, the Examiner should withdraw this rejection.

The Examiner has also rejected claim 1 under 35 U.S.C. 102(b) as being anticipated by Lowe, III et al., U.S. Patent No. 4,831,031, on the grounds that the reference discloses similar compounds in combination with a viscosity agent "ethanol". Applicant is frankly at a loss to understand the Examiner's rejection on this point. The particular cite to ethanol in Example 1, line 49, is a reference to a specific preparation of an example in that patent in which ethanol is used as a solvent. Applicant is at a loss to understand how this reference refers to a viscosity agent. Applicant, therefore, respectfully traverses application of anticipation on these grounds that the compound of Example 1 in the Lowe reference is not a representation of a depot formulation.

Rejections under 35 U.S.C. 103

The Examiner has rejected claims 1-3, 6-7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Tsai et al. in view of Johnson et al. The Examiner stated that Tsai et al. does not teach a cyclodextrin, but that Johnson et al. teaches a similar method and formulation and also a cyclodextrin. In the Examiner's view, it would have been obvious to a person of ordinary skill in the art to add the composition of Johnson et al. to the composition of Tsai et al. because Johnson et al. teaches similar composition for the same utlity. The Examiner stated that the motiviation to do so is supplied by Johnson et al. who teaches complexing agent such as cyclodextrins and organic solvents that may be used to increase the solubility, dissolution rate and stability of the formulation.

Applicants respectfully traverse this rejection. Neither Johnson et al. nor Tsai et al. pertains to solving the particular problem of a sustained release injectable depot formulation. It is true that Johnson et al. pertains to a method for solubilizing a genus of chemical molecules including ziprasidone. The method of solubilizing taught by Johnson et al. involves the use of cyclodextrins. Also, Tsai et al., like Johnson et al., pertains to providing new psychotherapeutic compositions and methods for treating psychological diseases. But there is no motivation to combine the particular elements of viscosity agent and solubilized drug provided by either reference, alone or in combination. Applicant submits that the combination of a solublized drug and a viscosity agent is actually counterintuitive. For arriving at a sustained release injectable

depot formulation, it is counterintuitive to use a *solublized* version a pharmaceutically active molecule (emphasis added). Accordingly, Applicant submits that the claimed invention is not obvious from Tsai et al. in view of Johnson et al.

The Examiner has rejected claims 15 and 16 under 35 U.S.C. §103(a) as being unpatentable over Johnson et al. in view of Arenson et al., WO 00/72847, on the grounds that Arenson teaches a combination of ziprasidone and a viscosity agent. Applicant respectfully traverses the Examiner's rejection on the grounds that Arenson is directed to oral formulations and specifically in that case the use of viscosity agents is taught as a supplement to the wedded particles so as to prevent settling of the active agent. Applicant respectfully refers the Examiner to page 2, lines 21-30 of that case, which refers to this phenomenon. Applicant, thus, respectfully submits that Arenson is an inappropriate reference in the current context. Applicant was seeking a method of preparing an injectable depot formulation with ziprasidone. Applicant is at a loss to understand how use of an agent to prevent settling in an oral formulation has any bearing on the problem confronted by the present inventor. The Examiner has not offered a single indication why one confronted with the problem confronted by the inventor would look to Arenson's disclosure of oral formulations to assist in the solution of his problem. Thus, Applicant respectfully requests that the rejection of Arenson be removed.

The Examiner also rejected claims 17 and 18 under 35 U.S.C. 103(a) as being unpatentable over Tsai et al. in view of Johnson et al. and Arenson et al. The Examiner cited Tsai et al. for the same propositions as asserted in the other rejections, namely for optionally combining a viscosity agent in a pharmaceutical composition comprising ziprasidone. The Examiner further stated that Tsai et al. teaches dosage form and duration such as 1-1000 mg/day and 1-1000 mg/month and 30 mg/kg/day once a day by month for a period of 6 weeks. The Examiner uses this to support a proposition that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to vary the duration of ziprasidone to optimize the effects desired.

Applicant respectfully traverses. At this point, Applicant's undersigned attorney wishes to point out that nowhere does Tsai et al. disclose the concept of "viscosity agents". True, Tsai et al. discloses numerous excipients which, *under certain circumstances and in the right quantities*, could serve as viscosity agents (although that is not mentioned in Tsai et al.). But that is far different from disclosing the motivation to incorporate a viscosity agent. Accordingly, it is difficult to see, for any of the Examiner's rejections, how Tsai et al. advances any solution that involves use of a viscosity agent where the problem is achieving a sustained delivery of a pharmaceutically active substance via injectable depot. It is even more difficult to see how Tsai et al. advances any solution that uses a viscosity agent to the sustained delivery of ziprasidone, given ziprasidone's own unique formulation challenges. The Examiner has plucked out of particular excipients from lists of excipients recited in a patchwork of references to arrive at the claimed invention. The

chosen excipients are not even discussed in the cited references as having the function of a viscosity agent. This is hindsight. In the recent Supreme Court holding in KSR International Co. v. Teleflex, Inc. 82 USPQ2d 1385 (US Supreme Ct 2007) the court stated that a court will often have to look to (1) interrelated teachings of multiple patents; (2) the effects of demands known to the design community or present in the marketplace; and (3) the background knowledge possessed by a person having ordinary skill in the art. Although this analysis should be explicit, the court explained, it "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." But in the instant case, the Examiner has not provided any discussion of how the *interrelated* teachings of the cited references arrive at the claimed invention.

As noted above, the Examiner suggests that it is obvious to vary the duration of ziprasidone release to optimize desired effects. Applicant respectfully submits that the Examiner has merely stated a wish or desire for sustained release of ziprasidone without explaining how *achieving* this wish is taught by the cited references. For these reasons, Applicant requests that the Examiner reconsider and withdraw the obviousness rejection of claims 17 and 18, and also all of the obviousness rejections set forth in the February 1, 2007 Office Action.

The Examiner has also rejected claims 1, 2, 3, 13 and 14 under 35 U.S.C. §103(a) as being unpatentable over Johnson et al. in view of Chemical Abstracts 138:309 126 (Chem Abs 126) and Faour et al., U.S. Patent Publication 2002/0132005. The Examiner cites Chem Abs 126 for the proposition that different combinations of sodium carboxy cellulose polymers produced different time release data. The Examiner also cites Faour for the proposition that combinations of aryl-heterocyclic compounds and hydroxypropyl methylcellulose, hydroxyethylcellulose, and carboxymethylcellulose have viscosities between about 3 to 100,000 cps and states that one of ordinary skill in the art looking to avoid a large-dose risk factor in dispensing aryl-heterocyclic drugs would be motivated to use the water soluble polymer such as sodium carboxy cellulose with an expectation that the combination would give slow release of the aryl-heterocyclic.

Applicant respectfully traverses the Examiner's rejection. Although Faour et al. and Chem Abs 126 may recite certain cellulose polymers which may be used as viscosity agents, what is the reason for including a viscosity agent with a solubilized ziprasidone, such as the solubilized ziprasidone taught by Johnson et al.? As asserted above, Applicant submits that use of a *solubilized* ziprasidone with a viscosity agent is counterintuitive. Applicant respectfully directs the Examiner to the comparative and unexpected results discussed as Example 1, starting on page 8 of the specification. Specifically, a formulation of the present invention was compared against an "immediate release formulation comprised of solubilized ziprasidone, but no viscosity agent." Such a comparative formulation (i.e. Johnson et al.) "showed no depot effect, i.e. the serum concentration of ziprasidone was not quantifiable after 48 hrs; there was no sustained serum

concentration". The formulation of the invention on the other hand showed a serum concentration of 12.9+/-3.7 ng/ml. Thus, the evidence demonstrates that the addition of a viscosity agent significantly alters the properties of even a solubilized ziprasidone. For these reasons, Applicant respectfully requests that the Examiner reconsider and withdraw the obviousness rejection over Johnson et al. in view of Chemical Abstracts 138:309 126 (Chem Abs 126) and Faour et al., U.S. Patent Publication 2002/0132005.

In conclusion, Applicant submits that all pending claims are patentable, and respectfully requests that they be allowed to issue.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicant's undersigned attorney kindly invites the Examiner to telephone the number provided.

Respectfully submitted,

Date: July 2, 2007

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